PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
RP/PCT/99-4		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/BE99/00121	22/09/1999	22/09/1999
International Patent Classification (IPC) or national classification and IPC A61L27/54		
Applicant BAXTER INTERNATIONAL INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 21 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
05/04/2001	19.12.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Pa l Soto, R Telephone No. +49 89 2399 7346

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/BE99/00121

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-43	as originally filed				

Claims, No.:

1-46	as received on	03/12/2001	with letter of	29/11/2001	

Drawings, sheets:

1/2,2/2	as originally filed				

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-46
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-46
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-46
	No:	Claims	

2. Citations and explanations
   see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following document as **D4**:

   WO 89 06945 A (BIOMEDICAL DESIGN INC) 10 August 1989

2. The present application relates to:

(i) *a cardiac valve* which has a biological or biocompatible support associated to at least one compound having at least one ring of 6 carbon atoms with at least two hydroxyl groups (**claim 1**),

(ii) *the use of a support associated to at least one compound* as previously defined for preparing an animal or human implant (**claim 12**),

(iii) *a method for preparing an animal or human implant comprising a support*, wherein the implant is treated with a solution containing a compound as defined in claim 1, or wherein said implant is at least partially prepared from a polymer or copolymer compound or from a cross-linkable biocompatible compound at least partially treated with a compound as defined in claim 1, and wherein, following said treatment, said implant is sterilised and/or treated aseptically (**claim 21**),

(iv) *the use of at least one compound selected from the specified group* for the preparation of a pharmaceutical composition for treating or preventing calcification in a blood circuit (**claim 28**),

(v) *an implantable support* intended to be in contact with a biological medium, said support being associated to at least one such compound (**claim 32**),

(vi) *the use of an aqueous composition for stabilizing an implantable support* wherein the composition contains: (a) at least an aldehyde in mixture with a compound selected from the compounds of the specified formula or (b) a compound selected of the specified formula (**claim 41**), and

(vii) *the use of a kit for preparing a composition for stabilizing an implantable support*, said kit comprising a first bottle containing as a powder or in an aqueous solution, a compound of the specified formula, and a second bottle containing an aqueous solution containing an aldehyde and preferably a phosphate buffer, the content of the two bottles having to be mixed together for preparing the stabilising solution (**claim 46**).

3.1. The present application meets the requirements of the PCT with respect to novelty (Art. 33(2)) because none of the documents cited in the International search report discloses the cardiac valves, implantable supports, the methods and uses as claimed in the present application.

3.2. It should be noted that all those technical features preceded by the expressions "preferably", "advantageously", "particularly", "especially", "such as" and the like are regarded as having no limiting effect on the scope of the claims.

4.1. Claims 1-46 of the present application appear to meet also the requirements of the PCT with respect to inventive step (Art. 33(3)) for the following reasons.

4.2. **D4** (see the abstract and lines 5-33 on page 5), which is regarded as the closest prior art, discloses a method for preventing calcification of a prosthesis implanted in a mammal by covalently coupling an aliphatic carboxylic acid to the prothesis before implantation. The present application differs from **D4** in that the anticalcification agent associated to the implant is a compound having at least one ring of 6 carbon atoms with at least two hydroxyl groups.

4.3. Thus the **problem** to be solved by the present application is to provide an alternative method to treat prosthesis before they are implanted in order to prevent calcification. The **solution** provided by the present application, i.e. the association of the implantable support to at least one compound having at least one ring of 6 carbon atoms with at least two hydroxyl groups, is not obvious because neither **D4** nor another document of the prior art, alone or in combination, would prompt the skilled person to modify the solution disclosed in **D4** in the way proposed in the present application. Accordingly, an inventive step is recognised in the cardiac valves of claim 1, the implantable support of claim 32, as well as in the use or methods of claims 12, 21, 28, 41 and 46.

5.1. **Claims 1-27 and 32-46** meet the criterion set forth in Article 33(4) PCT because their subject-matter is susceptible of industrial application.

5.2. For the assessment of the present **claims 28-31** on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The

patentability can also be dependent upon the formulation of the claims. The EPO, for example, may allow the use of a known compound for the manufacture of a medicament for a new medical treatment.

Re Item VIII

Certain observations on the international application

6. Claim 24 does not meet the requirements of Art. 6 PCT for the following reason. The formulation of said claim reads "... the compound having... is selected from the group comprising...". It is not clear whether (i) this is an opened definition or whether (ii) the identity of the compound is limited to the list specified. The present opinion has been established assuming case (ii); claim 24 has been read in this respect as the rest of the claims, namely: "... the compound having ... is selected from the group *consisting of* ...".